ABSTRACT

Non-activated tissue-regeneration polypeptides (TRPs) and the preparation methods thereof are disclosed. The TRPs contain: a protein transduction domain (PTD) making the polypeptides to permeate a cell membrane without cell membrane receptors; a furin activation domain (FAD) which has at least one proprotein convertase cleavage site and which can be cleaved by the proprotein convertase and activate a tissue regeneration domain (TRD) in cells; and a tissue regeneration domain (TRD) which can be activated by the proprotein convertase cleavage of the FAD to stimulate the growth or formation of tissues or to induce the regeneration of tissues. The TRPs can be practically mass-produced by the culture of bacteria, such as recombinant *E. coli*, and are in a non-activated state before *in vivo* administration. Thus, their production cost is only a few tenths of the prior active proteins having uses similar thereto, and processes for their separation, purification, handling, storage and administration are significantly simple and convenient. The *in vivo* administration of the TRPs can stimulate the formation or regeneration of tissues, such as bones or cartilages, or improve the fibrosis and cirrhosis of organs, such as kidneys, liver, lungs and heart by pharmacological mechanisims completely different from those of prior rhBMPs or TGF-β proteins. Accordingly, the TRPs will be useful as drugs having new mechanisms.